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Advanced Optical Technologies for Defense Trauma and Critical Care

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14. ABSTRACT

Work under this center grant consisted of 7 projects directed toward the development and translation of biomedical photonics technologies to address Joint Force Health Protection (JFHP) capability gaps for combat trauma and critical care that have been identified by the Secretary as requiring medical R&D. These efforts include Diffuse Optical Spectroscopy (DOSI) detection for hemorrhagic shock, cytochrome c oxidase, and dehydration; Optical Coherence Tomography (OCT) for evaluation of airway injury; Spatial Frequency Domain Imaging (SDFI) and Laser Speckle Imaging (LSI) for imaging of burns, wounds and reconstructive surgery; a continuous, real time, minimally invasive Lactate/pCO2/pO2 patient sensor; Multiphoton Microscopy (MPM) for imaging wound biofilms, and the development of innovative technologies for the study of the response of nervous system cells to injury.

15. SUBJECT TERMS

Hemorrhagic shock, dehydration, cytochrome c oxidase, DOSI, airway injury, OCT, MPM, wound imaging, burn imaging, lactate sensor, pCO2 sensor, wound biofilms, traumatic brain injury

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Final Performance Report

PRINCIPAL INVESTIGATOR: Michael W. Berns, Ph.D.

INSTITUTION: University of California, Irvine

GRANT TITLE: Advanced Optical Technologies for Defense Trauma and Critical Care

PERIOD: 15 November 2013 – 31 December 2016

GRANT NUMBER: FA9550-14-1-0034

Program Manager Change: Dr. Patrick O. Bradshaw

No Cost Extension: From 14 Nov 2016 to 31 Dec 2016

The following projects were conducted with funding under this grant:

PROJECT 1: Critical Care Monitoring: Cytochrome c Redox DOS and Lactate – pCO_2 Biosensor (Botvinick, Brenner)

Objectives:

The objectives of this study were to:
1) Validate the accuracy of the novel, continuous, Subcutaneous Metabolite Monitor (cSMM) lactate and pCO2 measurements as compared to blood pCO2 and lactate levels,
2) Correlate the degree of CcOx redox state changes provided by non-invasive DOS with the onset and extent of lactate formation/anaerobic metabolism in our established:
   i) Rabbit critical hemorrhage and resuscitation models.
   ii) Rabbit lethal and sub-lethal CN poisoning and treatment models.

Accomplishments:

Lactate biosensor: Over the course of this 3-year grant, the lactate sensor has been refined for ease of manufacture. An initial 40 sensors were made, and the process was shown to be repeatable. Implanted lactate sensors were tested in rabbit cyanide poisoning models, and shown to be 89% accurate as compared to standard blood lactate measurements. Continuous, real-time lactate sensors were additionally implanted in a pig undergoing smoke inhalation and burn studies at USAISR. Continuous measurements from the implanted sensor consistently measured within 0.2 mM lactate compared to gold standard point of care blood lactate measurements over the course of 26 hours. The electronic unit for reading and analyzing implanted lactate sensor signals has been refined for clinical use. The unit for

reading lactate sensor values was converted to a single electronic chip that can be taped in adhesive bandage form to the skin for clinical use.
The lactate sensor was compared to DOS cytochrome c oxidase redox state changes in cyanide, hydrogen sulfide and smoke/cyanide treated rabbit models. Tissue lactate changes closely paralleled those of DOS-determined Cyt c Oxidase redox changes, with relatively short time lag throughout CN poisoning and reversal with antidotes.

In the most recent study year, the electronic backend of the sensor was reduced in size, proven to be repeatable, and its design was locked. Documentation of the electronic backend design and software was created as is required by FDA for future filings. The housing for the detector that sits on the skin surface was redesigned for ease of use for a planned clinical study. An interface to connect the detector housing to the insertion device was also designed and prototyped using 3D printed parts. The insertion device allows for a standard 18 gauge IV catheter to be inserted through it to deliver the sensor to the exact location under the skin surface needed to obtain perfect alignment of the sensor with the detector housing above the skin (Figure 1). The tethered sensor design was also changed to allow for it to fit inside the 18 gauge catheter. Designs were made that allowed for insertion into a smaller, 23 gauge catheter, but these proved to be too thin to be threaded into the catheter consistently, so in practice the 18 gauge design worked better and was used for the clinical study. Sterilization and testing of sterilized units was also performed.

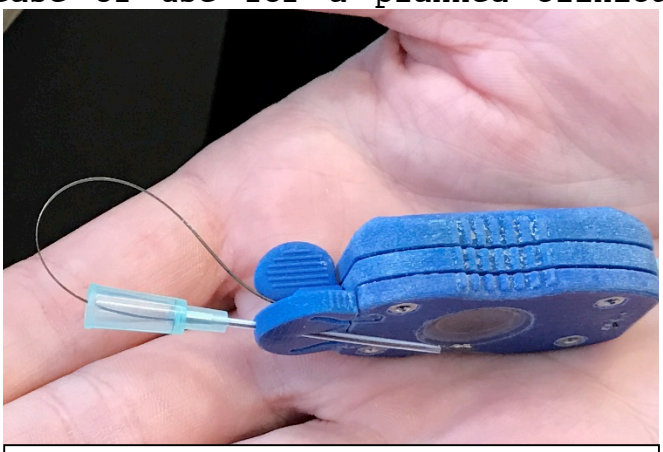


Fig. 1. Clinical Unit: Lactate Biosensor

Outside the scope and support of this grant, we were able to assemble sensor units in a clean room environment and batch-sterilize them following FDA guidelines for non-significant risk investigational devices. This allowed us to obtain IRB approval at UCI to perform a small clinical study to assess the lactate biosensor in human volunteers. Also outside the scope of this grant and without DoD funding we then performed the approved small clinical study to assess the feasibility of the lactate sensor in healthy human volunteers. The study involved insertion of the lactate sensor onto the lower back of the subject and placement of an IV catheter to take blood samples. After placement subjects were asked to pedal on a stationary bike at increasing loads to increase their work effort and subsequently

increase their lactate levels. Continuous measurements from our lactate sensors were compared to blood lactate measured by gold-standard bench-top analyzers and found to be in the accuracy range specified in the clinical protocol as acceptable.

Student Theses:

Dr. John Weidling, Ph.D. student with Dr. Elliot Botvinick, successfully defended his thesis at a seminar entitled "Transdermal Micro-implant for Critical Care Monitoring" on November 6, 2014. The thesis defense announcement and abstract is available at http://department-lists.uci.edu/pipermail/bme-graduates/2014-November/000017.html

Publication of the Dr. Weidling's completed thesis document, entitled "Transdermal Microimplantable Metabolite Sensor with Optical Communication" has been postponed pending the protection of intellectual property detailed within the thesis.

PROJECT 2: Non-invasive Methods for Detecting Acute Dehydration in Active Soldiers (Brenner)

Objectives:

1) Define the quantitative correlation between hydration status and DOS tissue water measurements over a range of dehydration and rehydration levels in an animal model.
2) Demonstrate and validate the capabilities of non-invasive DOS technologies to quantitatively monitor hydration status by measuring tissue water concentration during acute dehydration in humans during marathon running events, analogous to combat soldiers in vigorous, physically demanding scenarios.

Accomplishments:

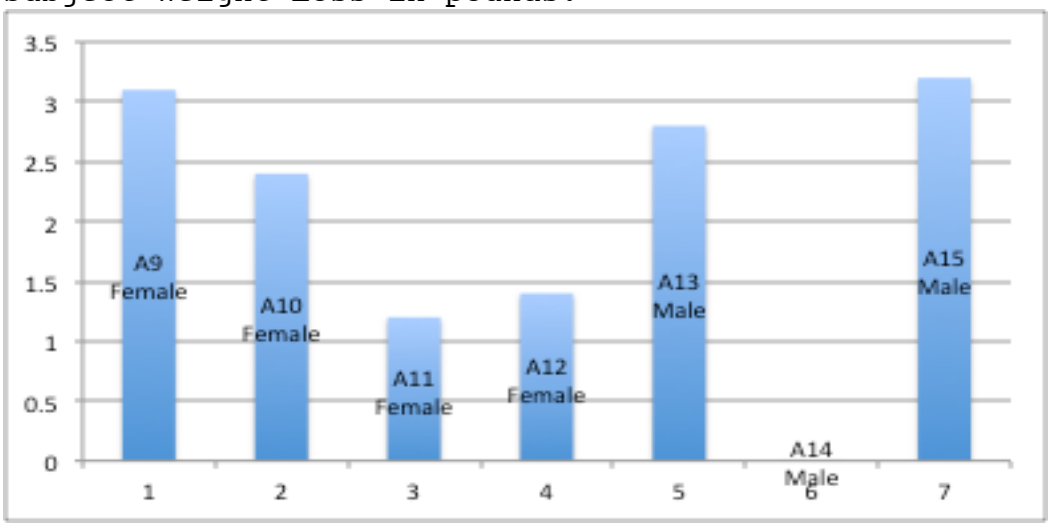
1) Completed eight rabbit experiments under the approved 36-hour dehydration and rehydration experimental protocol.
2) Completed UCI and AFOSR IRB protocol approvals for marathon trainee DOS study.
3) 7 healthy human subjects recruited.
4) DOS calibration phantoms and algorithms refined following initial 7 subject running study.
5) Seven additional human subjects were then enrolled in a sub-marathon running study. Three men and four women ranging in the ages from 45-65 were included.
6) DOS measurements were made on the bicep and calf muscles to determine changes in tissue water content resulting from 108-137 minutes of running.
7) In-vivo tissue concentrations of oxyhemoglobin, deoxyhemoglobin and lipid were measured pre and post run,

along with tissue water content, heart rate, SpO_2, body temperature and body weight.

Rabbit subjects (8) lost an average of 10.4% body weight over 36-hour dehydration period, and were then rehydrated. Rehydration was accomplished with D5W, and was detectable by DOS as a tissue water increase of 4-6%.

Results for the last seven human subjects indicated the ability of DOS to measure tissue hydration changes in some subjects.

Subject Weight Loss in pounds.



Subject Changes in DOS % Water

	Pre (%)	Post (%)
A09	34.0 ± 0.53	30.6 ± 0.53
A10	41.9 ± 0.12	35.6± 0.31
A14	37.7± 0.10	35.0 ± 0.82

Subjects A9, A10, and A14 showed a reduction in tissue water after exercise as measured by DOS (Data shown in Mean ± Standard Error).

Study Conclusions:

1) DOS can measure tissue water content as well as hemoglobin and lipid concentrations. Three out of seven subjects showed a reduction in tissue water content after rigorous workout.
2) While DOS can measure in-vivo changes of tissue water content, the measurement must be optimized further to ensure better chromophore concentration calculation.
3) "Optimal" balance between lipid and muscle (water) needs to be investigated further:
   a. Choice of measurement sites
   b. Source/detector separation
4) A 2-layer model of light propagation may help to eliminate the contribution/interference from the lipid layer.
5) This study demonstrates that in-vivo tissue water content may be detectible using DOS - with appropriate source-detector separation and tissue site selection to maximize spectroscopic content.
6) Additional subjects completing longer distance/time runs continue to be enrolled to validate findings, optimize measurement and analytical techniques, and examine a wider range of conditions.
7) Improved approaches for standardizing for regional variability in measurement and tissue lipid/muscle will be needed before this technology will be clinically applicable.

Student Theses: None

Project 3: Wide-field Functional Imaging for Assessment of Burns and Wound Healing (Durkin, Choi, Tromberg)

Objectives:

1) Conduct Wide-field Functional Imaging (WiFI) studies to non-invasively assess burn severity and wound healing in preclinical animal models (rat and porcine).
2) Develop metrics of burn severity, based on WiFI Data. The goal is to develop predictive WiFI-derived burn severity indices based on physiologically relevant information including burn thickness, inflammation and perfusion (tissue oxygen saturation), blanching (total hemoglobin concentration), collagen denaturation/remodeling (scattering), and hydration/edema (tissue water fraction).
3) Conduct clinical measurements of burn severity using WiFI-derived burn severity metrics by imaging burn patients admitted to the UC-Irvine Regional Burn Center and apply burn assessment metrics developed under Objective 2. We have an

IRB-approved protocol that enables clinical WiFI measurements in collaboration with Nicole Bernal (MD, UCI Burn Center).

Accomplishments:

We completed an initial evaluation of Spatial Frequency Domain Imaging (SFDI) and Laser Speckle Imaging (LSI) for assessing the severity of burn wounds in a swine model at US Army Institute for Surgical Research (USAISR). Burns of varying severities were created and their damage was verified using histology. We were able to correlate changes in reduced scattering coefficient (likely related to tissue denaturation) with burn severity as soon as one hour after the burn.

LSI was used to measure acute blood flow dynamics in a controlled rat burn model. Burn wounds of varying severity were created and could be distinguished by examining the reduction in blood flow as soon as three hours after the initial burn. This data demonstrates the potential role of LSI in the clinical assessment of burn wounds.

SFDI was used to extract tissue absorption and scattering properties over the short wavelength infrared (SWIR) range (850-1800 nm) for in-vivo rat burns. This approach has the potential to provide enhanced access to water and lipid information which previously has been difficult to obtain.

We have developed and implemented new techniques for SFDI with the potential of dramatically increasing image acquisition speed and move towards real time determination of tissue composition.

We developed and validated a wide-field method for the real-time mapping of tissue absorption, scattering and blood flow properties over wide regions of tissue (15 cm x 15 cm) with high temporal resolution (50 frames per second). We demonstrated the ability to resolve high speed intrinsic physiological signals such as the heart beat waveform and the buildup of deoxyhemoglobin associated with oxygen consumption.

We have designed and fabricated a new class of phantom that simulates the changes in scattering that typify burn wounds of various severities. This enables us to quantitatively evaluation iterations to instruments as they continue to develop.

Student Theses: None

Project 4: High Speed Long-Range Fourier Domain OCT Imaging of Inhalation Airway Injury (Chen)

Objectives:
The objective of the project is to develop a high-speed long-range Fourier domain OCT system for imaging combat injury and wound healing.

Diagnosis of inhalation injury is a primary unresolved problem in modern burn care. Up to 20% of patients admitted to burn centers have smoke inhalation injury (SII) which leads to respiratory failure and increases the predicted mortality by 20-60% above that predicted by burn size alone. The goal is to accelerate the translation and clinical development of this platform technology by demonstrating the ability of this technology to assess response to therapy in large animal models at USAISR. We proposed to design, construct, and deliver a complete high-speed long-range system to USAISR in continuation of our collaboration with Drs. Andriy Batchinsky and Lee Cancio for animal studies, to demonstrate readiness for burn/smoke inhalation airway injury studies in patients with this technology.

The specific objectives of this proposal were to:
1) Integrate a new swept source laser to further increase imaging range.
2) Demonstrate *user-friendly* image acquisition capabilities (use by non-technical personnel).
3) Deliver a complete high-speed long-range OCT system to USAISR and collaborate with USAIR for animal studies.

Accomplishments:

We developed and delivered a new high-speed long-range OCT system to USAISR for imaging airway burn injury in animal models. The old long-range OCT system has an imaging range of around 20 mm at an A-line repetition frequency of 50 kHz. To increase the imaging speed and imaging range, we developed and tested a VCSEL based high-speed long-range OCT, which can achieve an imaging range of 100 mm at a speed of 200 kHz, enabling 3-D imaging of full airway within 2 second. The OCT imaging probe of the earlier system was too large to fit into a bronchoscope biopsy channel, so it had to be inserted into the airway next to the bronchoscope. The new probe design has been optimized to fit through the working channel of a commercial bronchoscope, which makes it much simpler and easier to use in a clinical setting. Finally, we have developed an automatic airway wall segmentation and thickness measurement for long-

range OCT. The algorithm has been incorporated into the new long range OCT system and delivered to USAISR.

In addition to technology development, we have conducted joint experiment with USAISR using the new system and probe to measure thickness of the mucosal layer following smoke inhalation injury in a large animal model. We have published a joint paper on "In vivo detection of inhalation injury in large airway using three-dimensional long-range swept-source optical coherence tomography," in the Journal of Biomedical Optics.

Finally, the technology has been translated for clinical imaging and characterizing full upper airway of obstructive sleep apnea patients supported by NIH grants.

Student Theses: None

Project 5: Fiberoptic Imaging Probe for In-vivo Detection and Monitoring of Smoke and Chemical Agent Injuries of the Upper Airways (Wilder-Smith, Potma)

OBJECTIVES: The long-term goal of this project was to develop a small probe that could be used with a wide range of imaging modalities to map tissue properties at a metabolic, chemical and microstructural level. Imaging performance was evaluated in a hamster model for oral inflammation, cancer and wound healing.

Specific Goals:

1) Design, construct, and test a new clinical miniature handheld scanning non-linear optical microscopy (s-NLOM) probe for rapid examination of large tissue volumes capable of mapping cellular features in the tissue down to a depth of 0.5 mm at 4 frames per second. The technologically novel aspects of this imaging system are (a) the clinical scanning capability, (b) enhanced imaging depth and wide field of view, while (c) retaining sub-cellular resolution. The device will be fiber-coupled, lightweight and portable, packaged for easy access to the naso-pharynx and other difficult to access spaces.

2) Develop an interface for the s-NLOM probe with inexpensive, robust, portable, commercially available femtosecond light sources, including fiber lasers. These rugged sources feature small footprints and are suitable for use in the field in the near future.

Accomplishments:

1. Probe design:
   Our early work focused on defining the most important probe performance parameters, and translating them into technical design and construction. Based on these parameters, we optimized the probe design using ZEMAX software, making technical improvements that permit high NA (0.7) and exceptionally wide field of view for visualization of larger tissue areas (Figure 1). Employing novel tight focusing and high efficiency collection of scattered signal approaches, we improved detection sensitivity at greater focusing depths, increasing imaging depth to almost 1mm (from 0.15mm), and scan speeds to 10 frames per second. Lateral resolution was <1um; axial resolution approximated 5um.

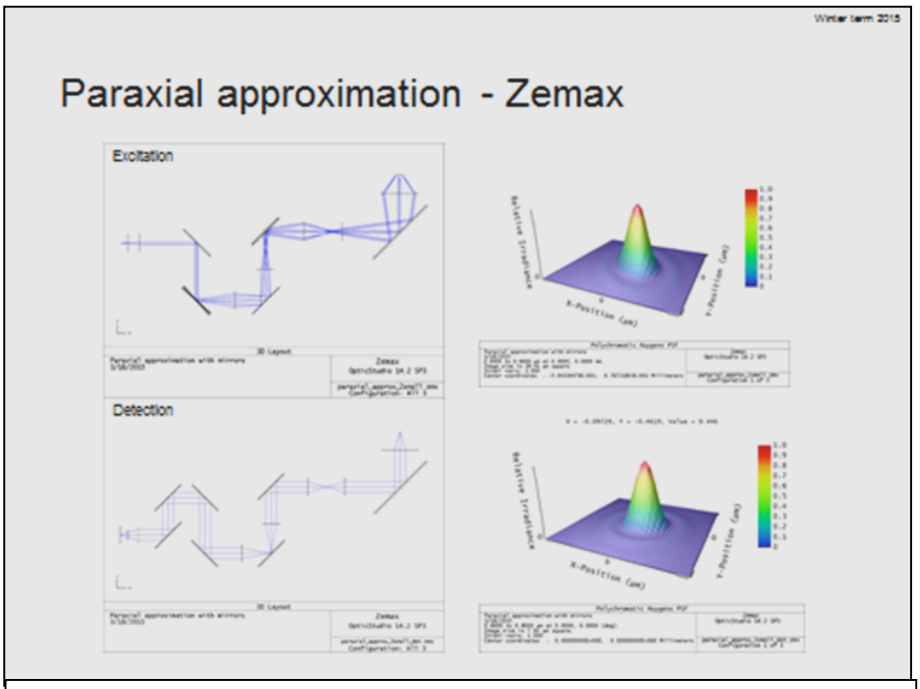


Fig. 1: ZEMAX modeling for probe design

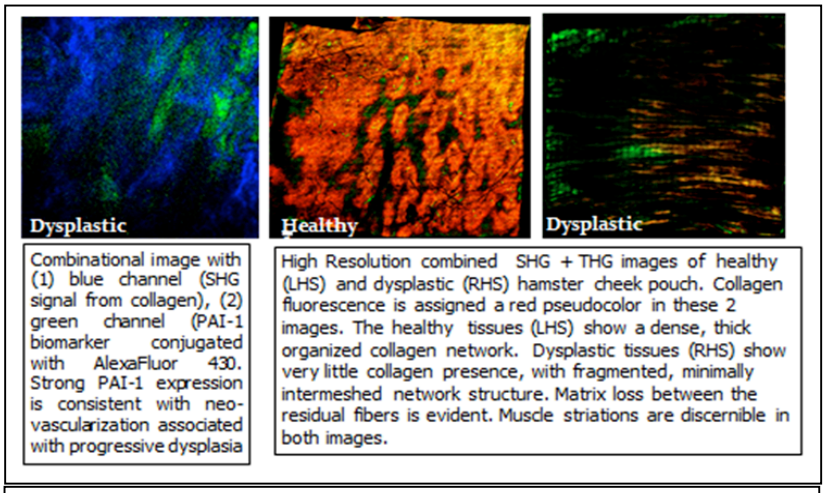


Fig. 2: NLOM imaging of healthy and dysplastic hamster cheek pouch

2. Imaging in hamster cheek pouch model:

a) We tested the probe in healthy hamster cheek pouch, and used the feedback to improve probe performance parameters,

especially its ability to image non-flat surfaces and acquire specific focal planes.

b) The modified probe was used to acquire multimodality images in hamster cheek pouch models for oral inflammation, infection and carcinogenesis (Figures 2, 3 and 4). A wide range of biomarkers for inflammation, infection, necrosis and carcinogenesis were mapped, and clear images showing presence, localization and concentration of biomarkers such as VEGF, EGFR and MMPs within the subsurface tissues of the oral mucosa were generated (Figure 2). Collagen presence was also mapped and changes in density, continuity and fiber properties were identified (Figure 2). In infected tissues, wound infection biofilm invasion of the wound was imaged (Figure 4). This technique permits unprecedented non-disruptive evaluation of wound biofilm behavior including tissue invasion.

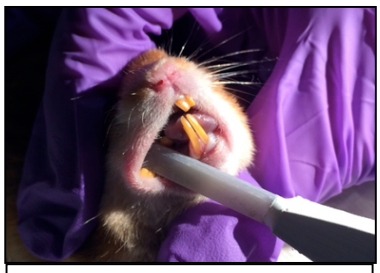


Fig. 3: NLOM imaging in the hamster cheek pouch

Fig. 4: 3-D NLOM images of wound biofilm growth and tissue penetration over time (0-100 hours. S-wound surface. Biofilm invasion of the tissue surface is first seen at 50h. Size bar = 500 um

Student Theses: Towards in vivo Nonlinear Optical Microscopy - Richa Mittal PhD thesis (overview attached).

Project 6: Wound Healing In Nerve Calls Following Laser-induced Shockwaves (Berns)

Objectives:

This project focuses on understanding nerve-healing following traumatic injury. The ultimate goal is to develop effective approaches to accelerate nerve healing following traumatic brain injury (TBI) and traumatic injury to the peripheral nervous system.

Two key aspects of repair of traumatic nervous system damage are: (1) the ability of damaged neurons to heal (repair the damage), and (2) the ability of non-neuronal cells (astrocytes) to remove the necrotic debris of dead cells. In addition to removal of the dead-cell debris, which itself is important to the healing process, we believe that the astrocytes facilitate the recovery of the damaged neurons, potentially through the release of chemicals that promote wound healing. By understanding the process of induced traumatic damage to the nervous system, as well as understanding the ability of the damaged tissue to repair, our ultimate goal is to develop mitigating strategies to facilitate and accelerate the repair of traumatic nerve damage.

The specific goals of this project during the past three years were:

1. Establish in-vitro cell culture systems to study the nervous system.

2. Perfect a laser-based system to induce shock wave and other non-linear physical damage to neurons and their associated astrocytes.

3. Study the damage and recovery mechanisms of individual cells and cell networks.

4. Integrate Fluorescence Resonance Energy Transfer (FRET) probes into the genomes of nerve cells in order to understand the molecular mechanisms of the cell response following exposure to the laser-induced shockwave.

5. Apply the results of our previous low light level bio-stimulation of wound healing to accelerate the repair of damaged nerves (leading to an eventual goal of an applied clinical deliverable).

Accomplishments:

1. <u>In-vitro model systems</u>
   We have successfully established several in vitro systems to study mammalian nerve cells. These are:(1) neurons from rat hippocampus, (2) astrocytes from rat brains, (3) neurons from mouse brains, and (4) dorsal root ganglia from rat spinal cord.

2. Laser-based shock-wave damage system

Two systems have been constructed and tested for the induction of specific shock-wave and non-linear damage to individual neurons and associated astrocytes. One system uses an 800 nm Ti:Sapphire femtosecond pulsed laser and a second system utilizes a 532 nm Nd:YVO4 diode pumped nanosecond laser (Figure 1). In combination with a Zeiss Axiovert inverted microscope and a CO_2 controlled stage incubator, nervous system cells were observed via time lapse imaging. Utilizing the computer program *Robolase* that was developed with previous AFOSR funding, we were able to visualize the interactions in real time, control the exposure of the laser, and target a specific area of the cell.

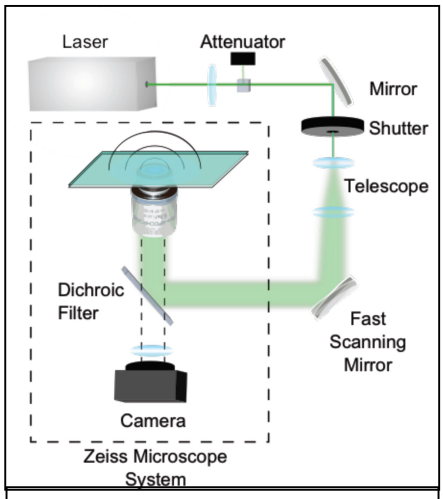


Fig. 1: Short-pulsed shockwave generating system.

3. Study the damage and recovery mechanisms of individual cells and cell networks

Using the system described above, we were able to damage a single cell and leave the neighboring cells unharmed. Cellular interactions were characterized by the formation of processes between cells and by subsequent phagocytosis (the healthy un-damaged cell engulfing the damaged/dead cell). Phagocytosis appears to be dependent on the type of connection present between the cells prior to laser exposure. Cells were categorized into two major categories: (1) direct contact with either other astrocytes or neurons (connected), or (2) those cells that had no direct contact with other astrocytes or neurons (non-connected). The connections can be via individual or multiple filopodia, or via a larger amount of shared plasma membrane. Connected cells had a higher chance of phagocytosing the laser-damaged (lysed) cell. Furthermore, the connected cells were more likely to phagocytose the cell if they were in a group as compared to those that shared no connection. Sixty-five percent of the connected cells reacted to the lysed cell by phagocytosing the cellular remnants (debris) while only 22% of the non-connected cells engulfed the dead/damaged cell. It should be pointed out that in an organ such as the brain or spinal cord, there will be connections between most of the cells. We found that astrocytes reacted similarly to laser-induced lysis of neurons. Lysis of neurons was induced by targeting two different cellular regions: the cell body and the axon. Similar to the astrocyte-astrocyte interaction, connected

cells had a higher chance of phagocytosing the axon than non-connected cells. In conclusion, this study suggests that astrocytes play a key role in phagocytosis of damaged nervous system cells (astrocytes and neurons). Parameters that can affect their ability to phagocytose include the amount of shared membrane between cells, as well as the location in the cell of laser-induced lysis. The study points out the importance of astrocytes in the process of wound-healing: they are key to cleaning up the debris of dead cells so that the tissue can heal normally. Future studies could focus on pharmacological stimulation of the astrocytes so that they accelerate healing following trauma.

4. Integrate Fluorescence Resonance Energy Transfer (FRET) into the genomes of nerve cells in order to study their response to shock-wave

Using the system depicted in Figure 1, we used laser-induced shockwave (LIS) and Forster Resonance Energy Transfer (FRET) biosensors to directly observe effects of shear stress on the different types of neurons. We have observed that neurons from the cortex of the brain in mice and rats along with dorsal root ganglia (DRG) from the spines of rats respond similarly to shockwave. Immediately following the shockwave, the neurons release internal calcium and quickly recover to attempt to return to their pre-shockwave calcium levels (see Figure 2).

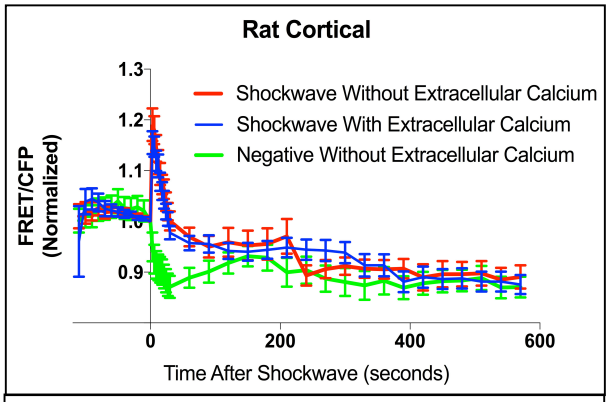


Fig. 2: graph of FRET-detected changes in calcium after shockwave.

We conclude that throughout these different neuronal types that there is a trend for internal calcium release to follow mechanical damage, indicating that it may be a part of the cell's natural repair or damage response pathway. This finding can be extrapolated to mammalian systems in general, and specifically to damage-recovery mechanisms following traumatic injury. The results of these studies were reported at the annual meeting of the American Society for Cell Biology (ASCB), and the Society of Photo-Instrumentation Engineers (SPIE).

5. Low light bio-stimulation to accelerate wound-healing.

We have established a new model to investigate the role of astrocytes in repair of brain injury. An established astrocyte cell line was utilized in vitro in a wound healing assay. The

addition of LED light at 635 nm at an average irradiance of 3 mW/cm^2 resulted in an increase in the velocity of astrocyte migration into the wound area. These preliminary results suggest that low level light biostimulation can be used to accelerate wound healing in a clinical setting. This could certainly have application to a battlefield military setting.

Student Theses:

"Laser ablation of single telomeres in mitosis: effects and consequences." - Silva, Barbara: PhD Thesis, UC Irvine, 2014. (Publications 24 and 25)

"Multimodal Wound-healing Acceleration" - Spitler, Ryan: PhD Thesis, UC Irvine, 2014. (Publications 26, 27 and 28)

"The use of optical scissors and optical tweezers in cell biology: sperm motility and nerve regeneration." - Hyun, Nick: MS Thesis, UC San Diego, 2014. (Publication 22)

Project 7: Diffuse Optical Spectroscopy in Evaluation of Interventions for Severe Hemorrhage (Tromberg)

Objectives:

Quantitatively monitor hemodynamics during hemorrhage and resuscitative endovascular balloon occlusion of the aorta (REBOA) using dual-channel diffuse optical spectroscopy (DOS).

Accomplishments:

In collaboration with USAISR, hemodynamics of Sinclair swine undergoing massive hemorrhage and REBOA were tracked in-vivo using a dual-channel DOS device. Multiple BLI personnel traveled to USAISR on 4 separate trips to install DOS technology and hardware/software upgrades, train USAISR operators, and participate in data acquisition. Over the past year, data from these trials was extensively analyzed in collaboration with UCI biostatisticians. Several invasively obtained conventional physiological parameters such as mean arterial pressure were found to significantly correlate with the non-invasively recovered DOS parameters during hemorrhage. However, during REBOA, these physiological parameters failed to fully describe tissue status in occluded regions, whereas DOS technology proved capable of providing continuous, real-time tissue hemodynamic feedback despite lack of blood flow and pressure. Results were reported as a poster presentation at the 2016 MHSRS conference

in Kissimmee, FL. Furthermore, a manuscript was finalized and submitted to the Journal of Military Medicine MHSRS Supplement.

With regards to instrumentation, we are committed to providing system upgrades resulting in increased sensitivity, speed, and reliability. An enhanced dual-channel DOS device, with a redesigned frequency-domain photon migration (FDPM) component, infrared-enhanced avalanche photodiode (APD), robust low-profile probe, and software update was delivered to USAISR.

Student Theses: None

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PATENTS AND DISCLOSURES
AFOSR FUNDED TECHNOLOGIES (2014 TO 2016)

Title: *Imbedded oxygen sensor for untet*hered assessment of oxyg*enation of implanted devices*
Inventors: E. Botvinick, J. Wiedling
UC Case: 2014-927-2
Status: U.S. Patent application filed 06/15/15.

Title: Continuous Analyte Sensor
Inventors: E. Botvinick, J. Wiedling, S. White
UC Case: 2013-017-3
Status: U.S. Patent application filed 08/06/15. PCT/US15/044063.

Title: *Method and apparatus for performing qualitative and quantitative analysis of burn extent and severity using spatially structured illumination.*
Inventors: A. J. Durkin, A. Mazhar
UC Case: 2012-137-2
Status: U.S. Patent application filed 01/24/14.

Title: *Method for extraction of spatial frequency information for quantitative tissue imaging.*
Inventors: K. Nadeau, A. J. Durkin, B. J. Tromberg
UC Case: 2014-468-2
Status: PCT filed 01/06/15 # PCT/US15/10278

Title: *Spatial Frequency Domain Imaging Using Custom Patterns.*
Inventors: T. B. Rice, S. Konecky, K. Nadeau, A. J. Durkin, B. J. Tromberg.
UC Case: 2011-663-2
Status: PCT filed 01/05/15 # PCT/UC15/10201.

Start Up Companies Based On Technologies Developed At BLI/UCI Under AFOSR Funding:

OCT Medical Imaging, Inc. (Irvine, CA)
Modulated Imaging, Inc. (Irvine, CA)
Cell Biosciences, Inc. (Palo Alto, CA)
First Scan Corporation (Portola Valley, CA)
Tamar Technologies, Inc. (Newbury Park, CA)
Universal Coherence Imaging (Irvine, CA)

AFOSR Deliverables Submission Survey

Response ID:7709 Data

1.

Report Type

Final Report

Primary Contact Email

Contact email if there is a problem with the report.

gpeavy@uci.edu

Primary Contact Phone Number

Contact phone number if there is a problem with the report

949-201-8277

Organization / Institution name

University of California, Irvine

Grant/Contract Title

The full title of the funded effort.

"Advanced Optical Technologies for Defense Trauma and Critical Care"

Grant/Contract Number

AFOSR assigned control number. It must begin with "FA9550" or "F49620" or "FA2386".

FA9550-14-1-0034

Principal Investigator Name

The full name of the principal investigator on the grant or contract.

Michael W. Berns

Program Officer

The AFOSR Program Officer currently assigned to the award

Patrick Bradshaw

Reporting Period Start Date

11/15/2013

Reporting Period End Date

12/31/2016

Abstract

Work under this center grant consisted of 7 projects directed toward the development and translation of biomedical photonics technologies to address Joint Force Health Protection (JFHP) capability gaps for combat trauma and critical care that have been identified by the Secretary as requiring medical R&D. These efforts include Diffuse Optical Spectroscopy (DOSI) detection for hemorrhagic shock, cytochrome c oxidase, and dehydration; Optical Coherence Tomography (OCT) for evaluation of airway injury; Spatial Frequency Domain Imaging (SDFI) and Laser Speckle Imaging (LSI) for imaging of burns, wounds and reconstructive surgery; a continuous, real time, minimally invasive Lactate/pCO2/pO2 patient sensor; Multiphoton Microscopy (MPM) for imaging wound biofilms, and the development of innovative technologies for the study of the response of nervous system cells to injury.

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Do you have any discoveries, inventions, or patent disclosures to report for this period?

Yes

Please describe and include any notable dates

See page 21 of the final report.

Do not see a place on this page to submit the DD882. Will forward to program manager.

Do you plan to pursue a claim for personal or organizational intellectual property?

Yes

Changes in research objectives (if any):

None

Change in AFOSR Program Officer, if any:

New program manager: Dr. Patrick Bradshaw

Extensions granted or milestones slipped, if any:

No cost extension 15 November 2016 to 31 December 2016

AFOSR LRIR Number

LRIR Title

Reporting Period

Laboratory Task Manager

Program Officer

Research Objectives

Technical Summary

Funding Summary by Cost Category (by FY, $K)

	Starting FY	FY+1	FY+2
Salary			
Equipment/Facilities			
Supplies			
Total			

Report Document

Report Document - Text Analysis

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Appendix Documents

2. Thank You

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